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(54) Title: NICKEL PHOSPHITE CATALYSTS (57) Abstract Methods for coupling aryl halides or aryl sulfonates to produce biaryls or polyaryls using novel nickel phosphite catalysts are provided.		

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NICKEL PHOSPHITE CATALYSTS

Field of the Invention:

This invention relates to nickel phosphite catalysts for coupling aryl halides or aryl sulfonates to produce biaryls or polyaryls.

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Background of the Invention:

The coupling of aryl compounds to form biaryl compounds or polyaryl compounds via carbon-carbon bonds is of great synthetic importance. A large number of methods are known to effect such couplings, including Ullman couplings of aryl iodides and bromides (see P.E. Fanta, "The Ullman Synthesis of Biaryls," *Synthesis*, 9, 9-21, 1974), coupling of aryl bromides and iodides with aryl boronic acids and esters using palladium catalysts (A. Suzuki, *Acc. Chem. Res.*, 15, 178, 1982), reductive coupling of aryl halides with magnesium via Grignard reagents using nickel catalysts (T. Yamamoto and A. Yamamoto, *Chem. Lett.*, 353-356, 1977), reductive coupling of aryl chlorides with zinc using nickel triphenylphosphine catalysts (I. Colon and D.R. Kelsey, *J. Org. Chem.*, 51, 2627-2637, 1986; and U.S. Patent No. 4,326,989) and oxidative coupling of phenols using iron

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1 (III) or air and copper catalysts (L. F. Fieser and M.
Fieser, Reagents for Organic Synthesis, Vol. 1, 390,
1967) ..

5 Each of the above-referenced prior art methods for
the coupling of aryl compounds has certain limitations.
The Ullman coupling generally results in low yields and,
for best results, requires aryl iodides, which are
expensive. Although coupling of aryl chlorides, which are
less expensive than aryl iodides and aryl bromides, has
10 been accomplished by Yamamoto et al via Grignard reagents,
the generally more expensive aryl bromides and iodides are
preferred. In addition, in the Yamamoto et al coupling
reactions, groups such as ketones and esters, which are
not stable to Grignard conditions, must be avoided,
15 thereby limiting the scope of useful reactions. While the
Suzuki coupling is the method of choice for cross-coupling
to form asymmetric biaryls, it uses expensive palladium
catalysts and boronic acid substrates, which makes the
process more expensive and, hence, less desirable.

20 Because aryl chlorides cost substantially less than
aryl bromides and aryl iodides, the nickel phosphine
catalyzed couplings disclosed by Colon et al are widely
used. In the Colon et al method, a nickel compound, salt,
or complex is reduced in situ with zinc powder in the
25 presence of a phosphine (specifically a triaryl phosphine)
to form an active nickel (0) phosphine catalyst. It is
theorized that in the triarylphosphine process, each of
the nickel species in the catalytic cycle is capable of
losing one or more of its phosphine ligands (L) to form
30 coordinatively unsaturated complexes. These equilibria
have been studied by Tolman (C.A. Tolman, W.C. Seidel, and
L.W. Gosser, *J. Am. Chem.*, 96, 53 (1974)). The formation
of unsaturated complexes is said to be essential at certain

1 parts of the cycle, so that the aryl halide may react.
However, during other parts of the cycle, unsaturated
nickel complexes may cause the formation of unwanted by-
products or may react to form inert complexes unable to
5 catalyze further coupling. It has been found in using
the Colon et al process that the concentration of
phosphine ligand must be kept between certain limits to
prevent the formation of unsaturated nickel complexes
which are too reactive and which lead to unwanted side
10 reactions. The typical range of concentrations is
approximately 0.2 to 0.5 M triphenylphosphine, 0.5 to 1 M
aryl halide, and 0.01 to 0.05 M nickel.

In view of the foregoing, it can be seen that in the
Colon et al. process relatively large amounts of
15 triphenylphosphine must be used in coupling reactions
compared to the amount of aryl halide substrate. Since
such large amounts of triphenylphosphine must be used,
recovery and purification of triphenylphosphine is
required to enhance process economics. Because of the
20 inefficiencies involved in the recovery, the cost of the
process is substantially increased.

In addition to the increased cost of the Colon et al
process due to the loss of triphenylphosphine, such
processes also result in unwanted by-products due to
25 abstraction of an aryl group (Ar') from the phosphine
 $P(Ar')_3$. The abstracted aryl group can couple to aryl
halide (ArX), giving an undesired by-product $Ar-Ar'$, for
example. While increasing the concentration of phosphine
ligand can suppress (but not eliminate) this undesired
30 side reaction, increasing the phosphine concentration
further increases the loss of triphenylphosphine, thereby
increasing the overall process cost.

1 Aryl sulfonates react in a fashion similar to aryl
halides and may be coupled using nickel phosphine
catalysts such as that of Colon et al., for example, see
the work of Percec et al. (V. Percec, J-Y. Bae, M. Zhao,
5 and D. H. Hill, *J. Org. Chem.*, 1995, 60, 176-185; and U.
S. 5,241,044, issued August 31, 1993.)

There is a need in the art for economical catalyst
systems which can be used in reactions which couple aryl
halides or aryl sulfonates to form either biaryl or
10 polyaryl compounds and which enhance the economics of the
process while reducing or substantially eliminating by-
product formation.

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1 Summary of the Invention:

 An economical method for coupling aryl halides or
aryl sulfonates to form biaryl or polyaryl compounds is
provided which minimizes by-product formation. The method
5 comprises the steps of (1) providing an aryl sulfonate
non-limiting examples of which include an aryl
methanesulfonate (aryl mesylate), an aryl
trifluoromethanesulfonate (aryl triflate), an aryl
phenylsulfonate, an aryl tolylsulfonate (aryl tosylate),
10 an aryl fluorosulfonate, and an aryl
fluorophenylsulfonate; or an aryl halide selected from the
group consisting of an aryl chloride, an aryl bromide, and
an aryl iodide, (2) contacting the aryl sulfonate or aryl
15 halide in an anhydrous aprotic solvent with a catalyst
mixture comprising a nickel compound or complex, a
phosphite ligand, and a reducing metal to thereby form the
biaryl or polyaryl compound.

 The coupled products provided in accordance with this
invention can be used, inter alia, as monomers for
20 subsequent polymerization, as high boiling heating fluids,
as plasticizers for plastics and as chemicals in
pharmaceutical intermediates.

 In one preferred embodiment of the present invention,
the aryl halide has the formula:



 wherein X is independently selected from the group
consisting of Cl, Br, and I; m is 1 or 2; and Ar is
selected from the group consisting of:

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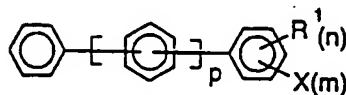
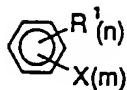


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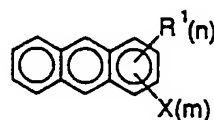
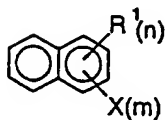


The aryl halide will have the general formulae:

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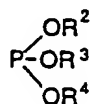


wherein p is 0 - 100, and R^1 is independently alkyl, alkene, aryl, alkoxy, aryloxy, amine, amide, fluoroalkyl, fluoroaryl, ketone, ester, formyl, cyano, fluoro, imide, sulfone, thioether, and the like. X and R^1 can be on any of the fused or multiple rings, and one to three CH units in any aromatic ring of each such Ar group can be replaced by a nitrogen atom. Any hydrogens of the aryl group may be substituted by R^1 substituents; therefore, n is 0-5 for phenyl, 0-7 for naphthyl, 0-9 for anthracenyl, 0-9 for biphenyl, and so on. Furthermore, where $m = 2$, the two halides are at positions on the Ar group other than ortho to each other.

Other aryl halides that can be coupled in accordance with practice of the present invention will be apparent to one skilled in the art, including but not limited to binaphthyl halides, phenylnaphthyl halides, phenanthryl

1 halides, branched aryl halides, such as triphenylbenzene
 halides, and the like. Additionally, the aryl halides may
 be heteroaryl halides, wherein each ring of the aryl group
 may have one to three nitrogen atoms. Non-limited
 5 examples of heteroaryl halides are 2-chloropyridine,
 3-chloropyridine, 4-chloropyridine, haloquinolines,
 including the mono- and di-chloroquinolines,
 haloquinazolines, haloquinoxalines, halopyrazines, and the
 like.

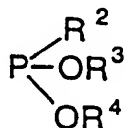
10 In one embodiment of practice of the present
 invention, the phosphite ligand has the formula:



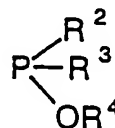
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wherein R^2 , R^3 , and R^4 are independently selected from the
 groups consisting of C_1 to C_{22} alkyl, C_6 to C_{24} aryl,
 alkaryl, and aralkyl.

20 In another preferred embodiment of practice of the
 present invention of coupling aryl halides to form biaryl
 or polyaryl compounds, the aryl halide is contacted in an
 anhydrous aprotic solvent with a catalyst mixture
 comprising a nickel compound, a reducing metal and a
 25 ligand selected from the group consisting of:



and



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wherein R^2 , R^3 , and R^4 are as defined above, to thereby
 form said biaryl or polyaryl compound.

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1 In yet another preferred embodiment of the present
invention, a mixture comprising an aryl halide, a nickel
compound or complex, and a phosphite ligand is prepared in
an anhydrous aprotic solvent containing an electrolyte.
5 The mixture is placed in an electrochemical cell
comprising a cathode, and the aryl halide is cathodically
reduced to form the biaryl or polyaryl compound.

 The present invention also defines a catalyst
composition useful for aryl halide or aryl sulfonate
10 coupling reactions. The composition includes a nickel
compound or complex, a phosphite ligand, and a reducing
metal selected from the group consisting of aluminum,
magnesium, and zinc, and an optional promoter selected
from chloride, bromide and iodide salts, wherein the molar
15 ratio of ligand to nickel is between 1 and 10, and the
molar ratio of reducing metal to nickel is between 1 and
10,000.

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1 Detailed Description:

 This invention provides an efficient and economical method for coupling aryl halides or aryl sulfonates to form biaryl or polyaryl compounds. The method includes
5 the steps of (1) providing an aryl sulfonate non-limiting examples of which include an aryl methanesulfonate (aryl mesylate), an aryl trifluoromethanesulfonate (aryl triflate), an aryl phenylsulfonate, an aryl tolylsulfonate (aryl tosylate), and an aryl fluorophenylsulfonate; or an
10 aryl halide selected from the group consisting of an aryl chloride, an aryl bromide, and an aryl iodide, (2) contacting the aryl sulfonate or the aryl halide in an anhydrous aprotic solvent with a catalyst mixture comprising a nickel compound or complex, a phosphite
15 ligand, an optional promoter selected from salts of chloride, bromide and iodide, and a reducing metal to thereby form the biaryl or polyaryl compound.

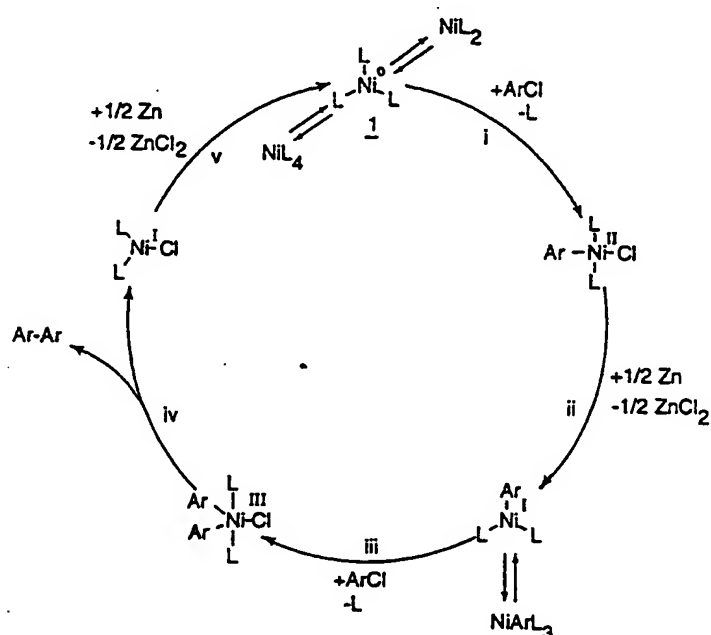
 As used herein, the term "aryl halide" includes aryl groups with a single halide substituent, as well as those
20 which include two halide substituents. When the aryl halide has one halide substituent, a biaryl compound is formed. When the aryl halide has two halide substituents, a polyaryl compound is formed.

 Similarly, the term "aryl sulfonate" includes aryl
25 groups with one or two sulfonate substituents. When the aryl sulfonate has one sulfonate substituent, a biaryl compound is formed. When the aryl sulfonate has two sulfonate substituents, a polyaryl compound is formed.

 A key to the development of the process of the
30 present invention was the surprising discovery that complexes of phosphites and nickel catalyze the reductive coupling of aryl halides. It was also surprisingly found (1) that the concentration of the phosphite ligand

required to effectuate the aryl halide reactions is lower than the concentration of phosphine ligand when triarylphosphine catalyst systems are used, and (2) that constituent groups are not abstracted from the phosphite moiety into the aryl chloride substrate, as is the case with phosphine catalyst systems. Thus, the use of phosphite catalyst systems is more economical and results in less undesirable by-product than is the case when phosphine systems are used.

While not wishing to be bound by theory, the following catalytic cycle, where L is phosphite, is consistent with the known behavior of the catalyst systems of the present invention.



In the presence of the phosphite ligand L, the nickel salt, compound or complex that is added initially is

1 reduced to a Ni(O) phosphite complex 1. The Complex 1
(the NiL_3) species is in equilibrium with the NiL_4 and NiL_2
species as shown. In step i, complex 1 oxidatively adds
aryl halide to give a Ni(II) aryl complex. In step ii,
5 the Ni(II) aryl complex is reduced by Zn (or other
reducing agent) to give a Ni(I) complex which oxidatively
adds a second aryl halide in step iii. Although it is not
always shown explicitly, each Ni species in the cycle may
add or lose ligand. Product biaryl is formed in step iv
10 by reductive elimination to give a Ni(I) species which is
reduced again to 1 in step v.

It is thought that the differing behaviors of the
phosphine and phosphite ligands are probably related to
the stability and reactivity of the Ni complexes.
15 Phosphites are stronger pi acids than phosphines and give
more stable complexes with low valent metals, such as
nickel(0) but less stable complexes with higher valent
metals, such as nickel(II). For example, it is known that
tetrakis(triphenylphosphite) nickel(0) is very
20 stable. For nickel(II) the complex
bis(triphenylphosphine)nickel(II)chloride is stable and
isolable, but the corresponding triphenylphosphite
nickel(II) complex is not.

In one preferred embodiment, phosphites useful in
25 conducting the coupling reaction of the present invention
have the general structural formula:



1 wherein R^2 , R^3 , and R^4 are independently selected from the group consisting of C_3 to C_{22} alkyl, C_6 to C_{24} aryl, alkaryl, and aralkyl.

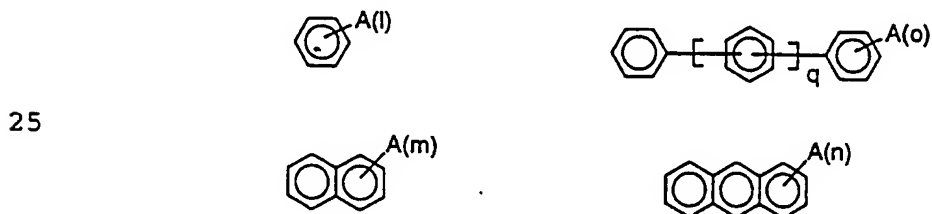
5 In the definition of C_6 - C_{24} aryl groups, the number of carbons (C) refers to the carbons in the ring structure itself. For example,

10  is a C_6 aryl;

 is a C_{10} aryl; and

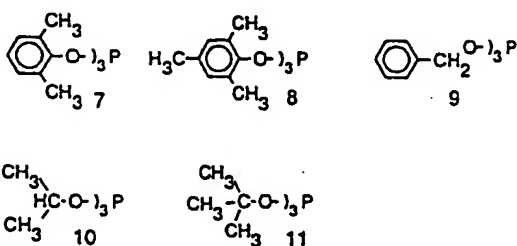
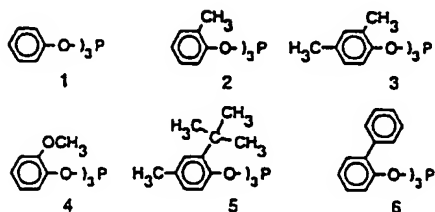
15  is a C_{14} aryl.

20 Non-limiting examples of aryl groups R^2 , R^3 , and R^4 useful in the phosphite ligands of the present invention are as follows:



30 wherein A is independently selected from the group consisting of C_1 - C_{22} alkyl, C_6 - C_{18} aryl, C_1 - C_{12} alkoxy, C_6 - C_{18} aryloxy, and F, and wherein $l = 0-5$, $m = 0-7$, $n = 0-9$, and $o = 0-21$; the A groups can be on any of the fused or multiple rings; and $q = 0-3$.

Preferred embodiments of phosphite ligands useful in practice of the process of the present invention include the following:



The phosphites having the structures shown above are known compounds, and in general the phosphites required for the catalysts of the present invention are readily synthesized by those skilled in the art from simple starting materials.

The size of the R groups on the phosphite ($P(OR)_3$) is an important consideration. If R is too small, e.g., methyl or ethyl, the Ni(O) complex will be too stable, and the catalyst will not be effective. Small R groups also favor dimeric Ni(O) and Ni(I) species which may not be catalytically active.

Additional phosphites with appropriate geometry useful in accordance with the present invention can be

1 deduced using the rules of cone angles known in the art.
Using the methods of Tolman et al to calculate cone
angles, catalysts comprising phosphites having cone angles
between about 120° and 185° will be effective catalysts.
5 Preferably, the phosphite will have a cone angle between
about 125° and 170°, more preferably between about 130°
and 160°, and most preferably between about 135° and 150°.
Tri-2-tolylphosphite, a preferred phosphite, has a cone
angle of 141°. The Tolman et al paper is incorporated
10 herein by this reference.

A phosphite may be tested for its coupling activity
using the following protocol. Coupling reactions of
4-chlorotolulene are run using the general conditions set
forth in Example 7 below, except that the amount of
15 phosphite is adjusted to give phosphite to nickel (L/Ni)
molar ratios of 2.01, 2.5, 3, and 4, and an internal
standard such as biphenyl is added at the beginning of the
reaction. The gas chromatograph (GC) yield of product
dimethylbiphenyl is measured at 1, 2, 4, and 16 hours.
20 Catalysts that give yields higher than approximately 10%
for at least one combination of the L/Ni molar ratio and
time are considered active. The dimethylbiphenyl yield
should be 10%, preferably 20%, more preferably 50%, and
most preferably at least 70%. Further experiments in
25 which the temperature (in steps of about 10 to 20°C), the
substrate to nickel ratio molar ratio (in increments of
about 25 to 50%), and the nickel concentration (in
increments of about 20 to 40%) are varied can be used to
optimize the time and yield of the reaction. These
30 conditions may also need to be modified when the same
phosphite ligand is used in coupling different substrates.

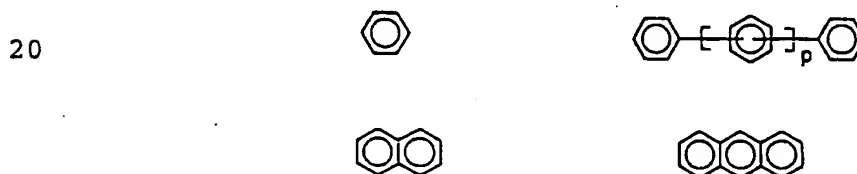
The aryl halides which may be coupled using methods
of the present invention include aryl chlorides, aryl

1 bromides, and aryl iodides. It was discovered that aryl
 fluorides are not reactive under the conditions of the
 process of the present invention. Aryl chlorides are
 preferred because they typically result in less side
 5 product produced by reductive replacement of the halide
 group with hydrogen. Additionally, aryl chlorides are
 usually less costly than aryl bromides or aryl iodides.
 Preferably, the aryl group does not bear substituents
 which react with the nickel catalyst or with the reductive
 10 metal. Such groups include nitro groups, free acid
 groups, or protic groups such as alcohol.

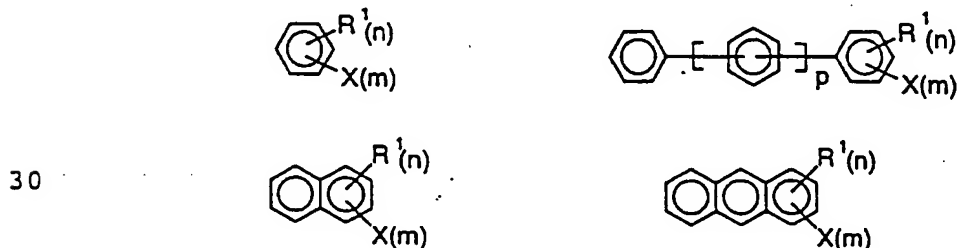
In a preferred embodiment, aryl halides which may be
 coupled using the methods of the present invention have
 the following general formula:



wherein X is independently selected from the group
 consisting of Br, Cl, I, m is 1 or 2, n is 0-10, and p is
 0-100; Ar is selected from the group consisting of:



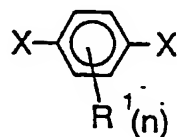
25 to provide aryl halides having the general structures:



1 wherein p is 0 - 100; R¹ is independently alkyl, alkene,
 aryl, alkaryl, aralkyl, aryloxy, amine, amide (-NR'COR" or
 -CONR'R"), fluoroalkyl, fluoroaryl, ketone (including
 5 alkyl ketone and aryl ketone), ester (-CO₂R' or -OCOR'),
 formyl (-COH), cyano (-CN), fluoro, imide, sulfone
 (-SO₂R), and thioether (R' and R" are alkyl or aryl);
 wherein X and R¹ can be on any of the fused or multiple
 rings; wherein one to three CH units in any aromatic ring
 of each such Ar group can be replaced by a nitrogen atom,
 10 and where m = 2, the two halides are at positions other
 than ortho to each other.

The aryl halides useful for coupling using the nickel
 phosphite catalysts of the present invention are either
 15 commercially available or readily synthesized by those
 skilled in the art. For example, chlorobenzoates,
 bromobenzoates, 2,3 and 4-chloroacetophenone, 2,3 and
 4-chlorobenzophenone, 2,3 and 4-chlorobenzonitrile,
 2,4-dichlorofluorobenzene, 2,5-dichlorotoluene, and the
 like are commercially available. Preparation of aryl
 20 chlorides and aryl dichlorides having ketone substituents
 may be accomplished by Friedel-Crafts acylation, as for
 example in U.S. Patent No. 5,210,313, issued May 11, 1993,
 which discloses preparation of dichlorobenzophenones.

In one embodiment, the aryl halide has the formula:



30 wherein X and R¹ are as defined above.

1 In another embodiment, the aryl halide has the
formula:



10 wherein X is as defined above and R' is alkyl or aryl.

In practice of the present invention, to form polyaryl compounds, aryl monohalides may be added to one or more aryl dihalides. The aryl monohalides act as endcappers and control the molecular weight of the polyaryl compound (the polymer) formed.

Non-limiting examples of R' groups are as follows:

alkyl groups are methyl, ethyl, propyl, isopropyl, tert-butyl, cyclohexyl, stearyl, and docosyl (-CH₂(CH₂)₂₀CH₃);

20 aryl groups are phenyl, biphenyl, naphthyl, anthracenyl, and diphenylphenyl;

alkaryl groups are o-tolyl, p-tolyl, m-tolyl, t-butylphenyl, dinonylphenyl, and poly(dioctylphenylene);

25 aryalkyl groups are phenyloctyl and naphthylmethyl;

C bound amides are N,N-dimethylaminocarbonyl (-CON(CH₃)₂), N,N-diphenylaminocarbonyl, piperidinecarbonyl (-CONCH₂CH₂CH₂CH₂CH₂), morpholinecarbonyl (-CONCH₂CH₂OCH₂CH₂), and N-methyl-N-phenylaminocarbonyl;

30 N bound amides are benzoylamino, N-methylacetylamino;

O bound esters are acetyloxy (-OCOCH₃) and benzoyloxy (-OCOC₆H₅);

1 C bound esters are methoxycarbonyl ($-\text{CO}_2\text{CH}_3$) and
phenoxycarbonyl ($-\text{CO}_2\text{C}_6\text{H}_5$);

alkoxy groups are methoxy, neopentyloxy, and
cyclohexyloxy;

5 aryloxy groups are phenoxy, naphthoxy, and
biphenyloxy;

alkene groups are groups that include a double
bond between two carbons of the group, for example vinyl,
and propenyl;

10 ketones are phenylketone (also called benzoyl),
naphthylketone (naphthoyl), methylketone (acetyl),
ethylketone (propionyl), tert-butylketone (pivaloyl),
isobutylketone, trifluoromethylketone (trifluoroacetyl),
methoxyethylketone, benzylketone, phenethylketone, 2,4,6-
15 trimethylphenylketone, pyridinylketone (nicotinoyl),
2-quinolinoketone, and 2-thiopheneylketone;

imides are phthalimide, fluorophthalimide, and
succinimide;

20 fluoroaryl groups are fluorophenyl and
perfluorophenyl; and

fluoroalkyl groups are trifluoromethyl,
perfluoro butyl, and 2,2,2-trifluoroethyl.

• In the reaction of the present invention, it is
typically sufficient to maintain the phosphite ligand to
25 nickel molar ratio in the range of about 2 to 10;
preferably in the range of about 2.4 to 5; more preferably
in the range of about 2.5 to 3.5; and most preferably in
the range of about 2.8 to 3.2. It appears that the
optimum ligand to nickel ratio is about 3. The useful
30 range of ligand to nickel ratio depends on the size of the
phosphite ligand. For small phosphites, such as
triphenylphosphite, the nickel (0) tetrakisphosphite
complex (NiL_4) is very stable, so that the phosphite to

1 nickel ratio must be kept below about 4. For larger
phosphites, such as tri-2-tolylphosphite, the NiL_4 complex
is destabilized, and larger amounts of phosphite may be
used; for example, up to 25 M equivalents of phosphite
5 relative to nickel or higher may be used, although at
these high levels, the reaction rate becomes slower.

In the systems of the present invention the amount of
phosphite relative to nickel is substantially less than
the concentration of phosphine to nickel in nickel
10 phosphine catalyst systems. For example, while in the
present systems the molar ratio of phosphite to nickel is
less than 10 and often may be less than 4 or 5, the molar
ratio of phosphine to nickel in nickel phosphine systems
is usually 5 to 10 equivalents and excess phosphine
15 improves yields.

It has been found that when using nickel/phosphite
catalysts, the phosphite ligand concentration can be kept
much lower than the phosphine ligand concentration when
nickel/phosphine catalyst systems are used. Additionally,
20 it has been found that the abstraction of aryl groups from
the phosphite ligand is completely precluded. This
reduces side reactions and resultant formation of
contaminating by-products that result from abstraction of
aryl groups when nickel phosphine catalyst systems are
25 used. Apparently, nickel does not insert into the
phosphite's O-aryl or P-O bonds as it does into P-aryl
bonds of phosphines. It is this insertion of nickel (O)
into the P-aryl bonds of phosphines, as has been described
by D.R. Fahey and J.E. Mahan (*J. Am. Chem. Soc.*, 98, 449
30 (1976)), which is a source of by-products in the
nickel/phosphine catalyst systems.

An additional advantage of phosphite ligands is
manifest during the work-up of the catalytic coupling

1 product. Since alkyl and aryl phosphites are easily
hydrolyzed and/or oxidized to water soluble phosphites and
phosphates the product is readily cleansed of phosphite
ligand by treatment with aqueous base. A similar process
5 is not possible with phosphines which do not hydrolyze so
easily.

In practice of this present invention, the nickel may
be introduced into the reaction mixture in any form which
can be reduced by the reducing agent to give a nickel(0)
10 phosphite complex. Zero valent nickel/ligand complexes
are also useful as long as the ligands are weak enough to
be displaced by the phosphite ligands. Non-limiting
examples of sources of nickel include nickel (II)
chloride, bromide, iodide, acetate, acetoacetate,
15 carbonate, sulfate, formate, toluene sulfonate, and
similar salts. Nickel complexes such as
bistriphenylphosphine nickel (II) chloride or
trisbipyridyl nickel (II) may be used. Nickel compounds
and complexes in the zero valent state may also be used
20 including nickel (0) biscyclooctadiene,
tetrakis(triphenylphosphine) nickel (0), nickel (0)
ethylene tris(triarylphosphite), and the like. Most
labile nickel compounds, i.e., nickel compounds where the
Ni is free to exchange a ligand, may be used. Counter
25 ions are not critical but should not be oxidants, such as
nitrate, or react with low valent nickel or the reducing
agent. The nickel compound will exchange its original
ligands or anions for phosphite ligands to form soluble
nickel phosphite complexes. The formation of the nickel
30 phosphite complexes may require the presence of the
reducing agent. Nickel compounds which bind nickel too
tightly, such as nickel tetraphenylporphyrin, are not

1 effective. Nickel (I) compounds, although rare, may also
be used.

Suitable reducing metals for use in practice of the
present invention are aluminum, manganese, zinc, and
5 alkaline earths such as calcium and magnesium. The metal
should be finely divided powders or dust, preferably with
a particle size less than about 100 mesh, and more
preferably with a particle size less than about 150 mesh.
The metal powder should be activated by treatment with
10 acid, followed by washing and drying. For example, highly
active zinc powder is made by treating zinc dust (-350
mesh) with HCl in diethylether, washing, drying and
resieveing (if necessary) to -150 mesh, where the minus
sign (-) indicates that all powder which goes through the
15 sieve is taken. Activated metals must be protected from
air before use. Zinc powder activated using the procedure
outlined in Example 1 set forth below is preferred.

Some reduction of substrate (i.e., replacement of
halide by hydrogen) also occurs by way of nickel
20 catalysis. Any water or protic solvent present, such as
alcohols or acids, will lead to reduction. Even in
anhydrous aprotic solvents, reduction may occur,
especially with substrates which are slow to react,
typically those containing electron donating groups like
25 alkoxy and alkyl placed ortho or para to the halide.

It may not be possible to eliminate such reduction,
and some minimum level of reduction of the substrate may
have to be tolerated. In general, it has been found that
catalysts with higher rates of product formation give less
30 reduction. It is the relative rates of coupling and
reduction that determine the product composition.

In another embodiment of practice of the present
invention, the reducing equivalents may be supplied

1 cathodically instead of by a reducing metal. The cathode
should be an inert metal such as platinum or steel, or an
inert non-metal conductor such as graphite. The solvent
5 must contain an electrolyte, such as an alkali or alkaline
earth halide, zinc halide, or alkylammonium halide. Most
common electrolytes are acceptable, including but not
limited to, alkali metal and alkaline earth metal salts,
alkyl ammonium halides, and zinc halides. The electrolyte
10 should be at least 0.01 M, preferably 0.1 M, and more
preferably 1 M in concentration. The anode may be an
inert metal or conductor such as platinum or carbon
respectively, or a sacrificial anode such as zinc or tin.
The appropriate range of applied potential or controlled
15 current will be apparent to one skilled in the art. In
general, the current will be controlled from about 10
ma/cm² to about 2 A/cm², preferably between about 100
ma/cm² to 1 A/cm², and more preferably between about 200
ma/cm² to about 600 ma/cm².

20 A divided cell is not necessary; however, anodic
products are more easily separated in a divided cell.
Where it is advantageous to avoid contamination of the
product by the oxidized form of the reducing agent,
electrochemical coupling in a divided cell is the method
of choice. The usual principles of electrochemistry
25 apply. Electrochemical techniques are generally preferred
at small scale production. In some cases, electrochemical
methods give better control over by-product formation
since reduction potentials may be set to values not
available with chemical reducing agents.

30 Preferably, a promoter is included in the catalyst
system of the present invention. Useful promoters are
chloride, bromide and iodide ions. The promoter ions may
be introduced as alkali or alkaline earth salts,

1 alkylammonium salts, or aluminum, manganese or zinc salts.
Bromide and iodide salts are preferred. The amount of
promoter may range from 0.01 M to 1 M, preferably from 0.1
5 M to 0.5M, and most preferably from 0.2M to 0.4M. Other
promoters useful in practice of the present invention
include sulfate, sulfonate, phosphate, and phosphonate
salts of alkali or alkaline earth metals, Al^{+++} , Mn^{++} , Zn^{++} ,
or alkyl ammonium. Bidentate aromatic heterocyclic
10 ligands such as bipyridyl, phenanthroline, and the like
can also be used as promoters.

The reaction solvents should be aprotic and must
dissolve the nickel phosphite catalyst to at least 0.0001
M in nickel, preferably to at least 0.001 M in nickel, and
most preferably to at least 0.01 M in nickel. Polar
15 solvents are preferred, including but not limited to
dimethylsulfoxide (DMSO), sulfolane, N-methylpyrrolidinone
(NMP), N,N-dimethylacetamide (DMAC),
N-cyclohexylpyrrolidinone, dimethylformamide (DMF),
N,N,N,N-tetramethylurea, and the like. These solvents can
20 be mixed with other aprotic solvents such as benzene,
butyrolactone, cyclohexane, diglyme, heptane,
propylenecarbonate, tetrahydrofuran, toluene, xylenes, and
other saturated aliphatic hydrocarbons, aromatic
hydrocarbons, or ethers.

25 The solvents useful in accordance with the present
invention are preferably anhydrous. The presence of water
leads to reductive replacement of the halide group with
hydrogen, and to deactivation of the catalyst. The
concentration of water should be kept below 1000 ppm,
30 preferably below 500 ppm, more preferably below 100 ppm,
and most preferably below 50 ppm. The concentration of
water may be reduced further to 40 ppm, 30 ppm, or even 20
ppm or 10 ppm, to avoid possible side reactions involving

1 water. Water may be reduced to these levels, for example,
by addition of activated molecular sieves, or by other
methods known in the art.

5 The reaction temperature for coupling should
typically be from about 0°C to about 120°C. The
temperature may be adjusted to optimize the product yield,
for example, temperatures of 50°C, 70°C, 90°C, or 100°C
may be preferred for a particular substrate.

10 The reaction pressure is not critical. Either
elevated or reduced pressure may be used as required. The
reaction must be carried out under inert atmosphere,
typically nitrogen. Other inert gases such as helium,
argon, and the like may also be used.

15 Reaction time is dependent on temperature,
concentration of catalyst and reactants, and amount of
promoter. Reaction time is typically between 2 and 24
hours. There is usually no maximum reaction time since
the product is usually inert to the catalyst.

20 The following examples are illustrative of the
present invention but are not considered limiting thereof
in any way.

EXAMPLE 1

25 Preparation of Activated Zinc Dust

Activated zinc dust is obtained after 2 washings of
commercially available 325 mesh zinc dust with 1 M
hydrogen chloride in diethyl ether (anhydrous) followed by
2 washings with diethyl ether (anhydrous) and drying in
30 vacuo or under inert atmosphere for several hours at about
100-200°C. If clumps form during drying the zinc dust is
re-sieved to -150 mesh. This material should be used

1 immediately or stored under an inert atmosphere away from
oxygen and moisture.

EXAMPLE 2

5 Coupling of N-(4-Chloro-2-benzoylphenyl)succinimide
using a nickel catalyst comprising
tri(2-methylphenyl) phosphite

A solution of anhydrous nickel chloride (49 mg,
0.38 mmol), sodium iodide (300 mg, 2 mmol), tri(2-
methylphenyl) phosphite (370 mg, 1.05 mmol) and N-(4-
10 chloro-2-benzoylphenyl) succinimide (2.79 g, 8.9 mmol) in
NMP (7 ml) was prepared in a glovebox and then stirred at
60°C for 3 hours. Activated zinc dust (1.6 g, 24.6 mmol)
prepared in accordance with the procedure of Example 1 was
added to the homogeneous green solution under helium. The
15 mixture was stirred at 60°C for 13 hours at 80°C for
another 6 hours. The reaction mixture was poured into
50 ml of water and filtered. The solid was collected by
filtration and then stirred in 20 ml of methanol for 2
hours. The suspension was filtered and the cake was
20 washed in the funnel with methylene chloride. Most of the
solid dissolved and the solvent in the filtrate was
evaporated. The solid was stirred in methanol and
filtered to give pure coupling product as crystals. The
crystals were air-dried to give 2.02 g 3,3'-dibenzoyl-
25 4,4'-succinimidobiphenyl (82%).

EXAMPLE 3

Coupling Reaction of 4-Chlorotoluene using a nickel
catalyst comprising tri(2-methylphenyl) phosphite

30 A mixture of anhydrous nickel chloride (50 mg,
0.39 mmol), sodium iodide (300 mg, 2 mmol), tri(2-
methylphenyl)phosphite (300 mg, 0.85 mmol) in NMP (5 ml)

1 was prepared in a glovebox and then stirred at 60°C for 1
hour 50 minutes. To the resulting green solution was
added activated zinc dust (1.5 g, 23 mmol) prepared in
accordance with the procedure of Example 1 under helium.
5 The mixture was stirred at 60°C and 4-chlorotoluene (1 g,
7.9 mmol) was added. After 17 hours, the reaction
temperature was raised to 80°C and the mixture was stirred
for another 7 hours. 4,4'-dimethylbiphenyl was obtained
in 97% yield by gas chromatography analysis of the
10 reaction mixture. The GC retention time of the dimer was
the same as that of dimer obtained using a literature
coupling method.

EXAMPLE 4

15 Coupling Reaction of 2-Chlorobenzophenone using a nickel
catalyst comprising tri(2-methylphenyl) phosphite

A mixture of anhydrous nickel chloride (50 mg,
0.39 mmol), sodium iodide (300 mg, 2 mmol), tri(2-
methylphenyl)phosphite (340 mg, 0.97 mmol),
20 2-chlorobenzophenone (1.01 g, 4.7 mmol) and zinc chloride
(1g, 7.4 mmol) in NMP (8 ml) was prepared in a glovebox
and then stirred at 60°C for 1 hour. To the solution was
added activated zinc dust (1.5 g, 23 mmol) prepared in
accordance with the procedure of Example 1 under helium.
25 The mixture was stirred at 60°C for 13 hours.
2,2'-dibenzoylbiphenyl was obtained quantitatively based
on GC analysis. The GC retention time of the dimer was
the same as that of dimer obtained using a literature
coupling method.

30

1

EXAMPLE 5

Coupling of 2-Chlorobenzophenone using a nickel catalyst comprising triphenyl phosphite

5 A solution of anhydrous nickel chloride (50 mg, 0.39 mmol), sodium iodide (300 mg, 2 mmol), triphenylphosphite (250 mg, 0.81 mmol), 2-chlorobenzophenone (1.01 g, 4.7 mmol) in NMP (5 ml) was prepared in a glovebox and then stirred at 70°C for 2 hours. To the solution was added activated zinc dust (1.6 g, 25 mmol) prepared in accordance with the procedure of Example 1 under helium. It was stirred at 70°C for 13 hours. 2,2'-Dibenzoylbiphenyl was obtained in 96% yield based on GC analysis. The GC retention time of the dimer was the same as that of dimer obtained using a literature coupling method.

15

EXAMPLE 6

Polymerization of 2,5-Dichlorobenzophenone Using A Nickel Catalyst Comprising Tri(2-methylphenyl)phosphite

20 A solution of anhydrous nickel chloride (47 mg, 0.36 mmol), sodium iodide (150 mg, 1 mmol), tri(2-methylphenyl)phosphite (700 mg, 1.99 mmol) and 2,5-dichlorobenzophenone (1.2 g, 4.8 mmol) in NMP (5 ml) was prepared in a glovebox and then stirred at 90° C for 40 minutes. Activated zinc dust (1.5 g, 23 mmol) prepared in accordance with the procedure of Example 1 was added to the homogeneous green solution under helium. The mixture was stirred at 90° C for 36 hours and then cooled to room temperature. The viscous solution was poured into 1 M HCl in ethanol. The solid was collected by filtration and was stirred in acetone for further purification. The polymer was obtained in 92% yield (0.79 g) after filtration and drying. Size exclusion chromatography (SEC) of the

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35

1 polymers relative to narrow polydispersity polystyrene
standards, for dilute solutions of the polymer in NMP
including 0.05 molar lithium bromide, indicated a weight
average molecular weight of 14,319.

5

EXAMPLE 7

Coupling of 4-Chlorotoluene using a nickel catalyst comprising Tri(2-phenylphenyl)phosphite

A solution of nickel chloride (50 mg, 0.39 mmol),
10 sodium iodide (300 mg, 2 mmol), tri(2-
phenylphenyl)phosphite (524 mg, 0.97 mmol) and 4-
chlorotoluene (1 g, 7.9 mmol) in NMP (5 ml) was prepared
in a glovebox and then stirred at 70°C for 2 hours.
Activated zinc dust (1.6 g, 25 mmol) prepared in
15 accordance with the procedure of Example 1 was added to
the solution under helium. The mixture was stirred at
60°C for 13 hours. Dimethylbiphenyl was obtained in 99%
yield based on GC analysis. The GC retention time of the
dimer was the same as that of dimer obtained using a
20 literature coupling method.

EXAMPLE 8

Coupling of 2-Chlorobenzophenone using a nickel catalyst comprising tri(2-phenylphenyl) phosphite

25 A solution of anhydrous nickel chloride (25 mg,
0.19 mmol), sodium iodide (60 mg, 0.39 mmol), tri(2-
phenylphenyl)phosphite (262 mg, 0.49 mmol),
2-chlorobenzophenone (2 g, 9.3 mmol) in NMP (5 ml) was
prepared in a glovebox and then stirred at 60°C for 2
30 hour. To the solution was added activated zinc dust
(0.75 g, 11.7 mmol) prepared in accordance with the
procedure of Example 1 under helium. It was stirred at
60°C for 11 hours. 2,2'-Dibenzoylbiphenyl was obtained in

1 99% yield based on GC analysis. The GC retention time of
the dimer was the same as that of dimer obtained using a
literature coupling method.

5

EXAMPLE 9

Coupling of 3-Chlorobenzophenone using a nickel catalyst
comprising tri(2-phenylphenyl) phosphite

A solution of anhydrous nickel chloride (50 mg,
0.39 mmol), sodium iodide (300 mg, 2 mmol), tri(2-
10 phenylphenyl)phosphite (524 mg, 0.98 mmol), 3-
chlorobenzophenone (2 g, 9.3 mmol) in NMP (5 ml) was
prepared in a glovebox and then stirred at 60°C for 2
hours. To the solution was added activated zinc dust
(1.4 g, 21.5 mmol) prepared in accordance with the
15 procedure of Example 1 under helium. It was stirred at
60°C for 4 hours. 3,3'-dibenzoylbiphenyl was obtained in
97% yield based on GC analysis. The GC retention time of
the dimer was the same as that of dimer obtained using a
literature coupling method.

20

EXAMPLE 10

Coupling of 4-Chlorotoluene using a nickel catalyst
comprising Tri(2-methoxyphenyl)phosphite

A solution of nickel chloride (50 mg, 0.39 mmol),
25 sodium iodide (300 mg, 2 mmol), and tri(2-
methoxyphenyl)phosphite (360 mg, 0.9 mmol) in NMP (5 ml)
was prepared in a glovebox and then stirred at 60°C for
1.5 hours. Activated zinc dust (1.6 g, 25 mmol) prepared
in accordance with the procedure of Example 1 was added to
30 the solution under helium followed by 4-chlorotoluene
(1 g, 7.9 mmol). The mixture was stirred at 60°C for 30
hours and at 80°C for another 15 hours. Dimethylbiphenyl
was obtained in 99% yield based on GC analysis. The GC

35

1 retention time of the dimer was the same as that of dimer
obtained using a literature coupling method.

EXAMPLE 11

5 Coupling of 2-Chlorobenzophenone using a nickel catalyst
comprising tri(2-methylphenyl) phosphite

A solution of anhydrous nickel chloride (50 mg,
0.39 mmol), sodium iodide (300 mg, 2 mmol), tri(2-
methoxyphenyl)phosphite (360 mg, 0.9 mmol), 2-
10 chlorobenzophenone (1.2 g, 5.6 mmol) in NMP (5 ml) was
prepared in a glovebox and then stirred at 60°C for 2
hour. To the solution was added activated zinc dust (1.4
g, 21.5 mmol) prepared in accordance with the procedure of
Example 1 under helium. It was stirred at 60°C for 12
15 hours. 2,2'-Dibenzoylbiphenyl was obtained in 97% yield
based on GC analysis. The GC retention time of the dimer
was the same as that of dimer obtained using a literature
coupling method.

20

EXAMPLE 12

Coupling of 4-Chlorotoluene using a nickel catalyst
comprising Tri(2-tert-butylphenyl)phosphite

A solution of anhydrous nickel chloride (50 mg,
0.39 mmol), sodium iodide (310 mg, 2.07 mmol), and tri(2-
25 tert-butylphenyl)phosphite (508 mg, 0.97 mmol) in NMP (5
ml) was prepared in a glovebox and then stirred at 60°C
for 1.5 hours. Activated zinc dust (1.5 g, 23 mmol)
prepared in accordance with the procedure of Example 1 was
added to the solution under helium followed by 4-
30 chlorotoluene (1g, 7.9 mmol). The mixture was stirred at
60-65°C for 15 hours. Dimethylbiphenyl was obtained in
99% yield based on GC analysis. The GC retention time of

1 the dimer was the same as that of dimer obtained using a
literature coupling method.

EXAMPLE 13

5 Preparation of 6-chloro-2-(4-fluorophenyl)-4-
phenylquinoline

A three-necked, 2 L round-bottomed flask equipped
with a thermometer, a mechanical stirrer and a
distillation unit fitted with a nitrogen inlet valve was
10 charged with 2-amino-5-chlorobenzophenone (695.0 g, 3.00
mol), and 4'-fluoroacetophenone (456.0 g, 3.30 mol),
p-tosic acid (47.62 g, 0.25 mol). The reaction mixture
was heated under nitrogen at 165°C (44 h). The yellow
4'-acetophenone that co-distilled with the water was
15 separated and reintroduced to the reaction mixture
throughout the heating period. The mixture was further
heated to 190°C (2 h). The mixture was cooled to 120°C
and was poured into 95% ethanol (10 L) while vigorously
stirring with a mechanical stirring rod set up. The
20 mixture was filtered and the precipitate was washed with
ethanol (1 L). The solid was dried in a vacuum oven at
80°C (16 h). Yield 969 g, 97%; mp 141.0-142.1°C.

EXAMPLE 14

25 Preparation of 6,6'-bis[2-(4-fluorophenyl)-4-
phenylquinoline]

A three-necked, 22 L round-bottomed flask equipped
with a mechanical stirred, a thermometer, and a nitrogen
inlet was charged with nickel chloride (27.38 g, 0.211
30 mol), tris(2-tolyl)phosphite (230.7 g, 0.655 mol), sodium
iodide (167.8 g, 1.12 mol), 6-chloro-2-(4-fluorophenyl)-4-
phenylquinoline (1713 g, 5.13 mol), and NMP (4.32 L). The
mixture was heated to 80°C under nitrogen (24 h). The

1 temperature of the reaction was lowered to 60°C and zinc
(455.7 g, 6.97 mol) was added. The reaction exothermed to
95°C, with the aid of a cooling bath for temperature
control. The mixture was stirred again at 80°C (24 h).
5 The mixture was heated further to 160°C until all of the
solids had dissolved and was then filtered hot through
Celite. The mother liquor was cooled to room temperature,
the crude product was collected by filtration, and the
crude product was washed with methanol (4 L). The solid
10 was dissolved in DMF (20 L) and subjected to another hot
filtration through Celite. The yellow crystals that
formed in the DMF filtrate were collected by filtration
and washed with methanol (2 L). The solid was dried in a
vacuum oven at 120 °C (16 h). Yield 1147 g, 74.9%.

15

EXAMPLE 15

Preparation of 6,6'-bis[2-(4-fluorophenyl)-4-
phenylquinoline] in a single pot from 2-amino-5-
chlorobenzophenone and 4'-fluoroacetophenone

20

A 250 mL, three-necked, round-bottomed flask fitted
with a mechanical stirring set-up, a short path
distillation apparatus, and a nitrogen inlet valve was
charged with 2-amino-5-chlorobenzophenone (Compound 3)
25 (17.4 g, 75.0 mmol), 4'-fluoroacetophenone (Compound 2)
(10.0 mL, 824 mmol), and tosic acid (0.505 g, 2.7 mmol).
The reaction was heated under nitrogen at 180°C (20 h) to
effect condensation and water removal. The temperature of
the reaction was lowered to 160°C, and potassium carbonate
30 (0.367 g, 2.7 mmol) was added. Toluene (100 mL) was then
added to the reaction and distilled away. This toluene
addition/distillation was repeated two times.

35

1 The temperature of the reaction was lowered to 80°C,
and the distillation unit was removed. The flask was
charged with nickel chloride (0.778 g, 6.00 mmol), sodium
iodide (2.43 g, 16.2 mmol), tris(2-tolyl)phosphite (6.77
5 g, 19.2 mmol), and NMP (63 mL), and the resulting solution
was stirred (18 h). The reaction temperature was then
lowered to 60°C, and activated zinc dust (6.59 g, 101
mmol) was added. After the exotherm had subsided (10
min), the reaction was allowed to stir at 80°C (16 h).

10 The temperature of the reaction was raised to 160°C
to dissolve the precipitate which had formed. The
reaction mixture was filtered while hot through Celite and
was allowed to cool to room temperature. The crude
product was collected by filtration and was washed with
15 ethanol. A second crop was collected from the mother
liquor and was washed with ethanol. The yellow product
was dried in a vacuum oven at 160°C (18 h). 12.0 g from
Crop 1 and 6.3 g from Crop 2 (Yield 73.1%).

 In a second embodiment aryl sulfonates are coupled to
20 biaryls and aryl disulfonate are coupled to polyaryls
using the same nickel phosphite catalyst and conditions as
for aryl halides. Thus, anhydrous dipolar aprotic
solvents such as NMP, DMF, and DMAC are suitable. The
reducing agents may be reducing metals such as aluminum,
25 calcium, magnesium, manganese, zinc and their alloys. The
reaction temperatures are from 25°C to 150°C, preferably
50°C to 100°C, and more preferably from 75°C to 90°C. The
reaction times are from 1 to 72 hours, preferably from 2
to 24 hours and more preferably from 4 to 16 hours. The
30 phosphite ligand to nickel molar ratio should be from
about 2:1 to about 4:1. The aryl halide to nickel ratio
should be from about 10:1 to about 10,000:1, preferably
from about 20:1 to about 1000:1, more preferably from

1 about 25:1 to 100:1, and most preferably from about 40:1
to about 80:1.

5 The above descriptions of various embodiments of
processes for coupling aryl halides or aryl sulfonates to
produce biaryls or polyaryls and the catalyst compositions
useful for such coupling reactions are provided for
illustrative purposes. Because of variations which will
be apparent to those skilled in the art, the present
invention is not intended to be limited to the particular
10 embodiments described above. Additionally, it should be
understood that any compounds or compositions that are not
described in the application as being useful for
practicing the invention, are not needed and the invention
can be practiced in their absence.

15 The scope of the invention is defined in the
following claims.

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1 WHAT IS CLAIMED IS:

1. A method of coupling aryl halides to form biaryl
or polyaryl compounds, the method comprising the steps of:
5 providing an aryl halide selected from the group
consisting of an aryl chloride, an aryl bromide, and an
aryl iodide; and

 contacting the aryl halide in an anhydrous
aprotic solvent with a catalyst mixture comprising a
10 nickel compound, a phosphite ligand, and a reducing metal
to thereby form said biaryl or polyaryl compound.

2. The method according to claim 1, wherein the
catalyst mixture additionally comprises a promoter
15 selected from the group consisting of chloride, bromide,
and iodide salts.

3. The method according to claim 2, wherein the
promoter is sodium iodide.
20

4. The method according to claim 2, wherein the
promoter is sodium bromide.

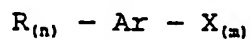
5. The method according to claim 1; wherein the
25 phosphite ligand to nickel molar ratio is in the range of
2 to 10.

6. The method according to claim 1, wherein the
phosphite ligand to nickel molar ratio is in the range of
30 2.4 to 5.

7. The method according to claim 1, wherein the
reducing metal is selected from the group consisting of

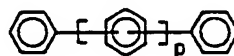
1 aluminum, calcium, magnesium, manganese, zinc, alloys of
aluminum, calcium, magnesium, manganese, and zinc, and
mixtures thereof.

5 8. The method according to claim 1, wherein the
aryl halide has the formula:



wherein X is independently selected from the group
consisting of Cl, Br, I, m is 1 or 2, and n is 0-10;

10 Ar is selected from the group consisting of:

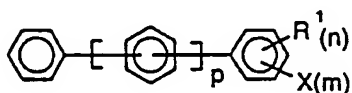
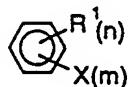


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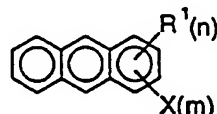
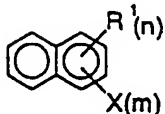


and the aryl halide has the formula:

20



25



wherein p is 0 - 100;

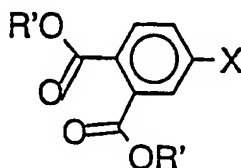
30 R is independently alkyl, alkene, aryl, alkoxy,
aryloxy, amine, amide, fluoroalkyl, fluoroaryl, alkyl
ketone, aryl ketone, ester, formyl, cyano, fluoro, imide,
sulfone, and thioether;

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1 wherein X and R can be on any of the fused or
multiple rings;

 wherein one to three CH units in any aromatic
ring of each such Ar group can be replaced by a nitrogen
5 atom, and where $m = 2$, the two halides are at positions
other than ortho to each other.

 9. The method according to claim 1 wherein the aryl
10 halide is

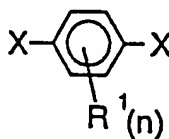


15 wherein X is selected from the group consisting of Cl, Br,
and I; and R' is alkyl or aryl.

 10. The method according to claim 1, wherein the
20 aryl halide includes two halide groups.

 11. The method according to claim 8, wherein the
aryl halide includes two halide groups para to each other.

25 12. The method according to claim 1, wherein the
aryl halide has the formula:

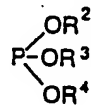


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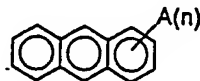
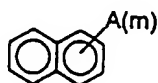
- 1 wherein X is independently selected from the group
 consisting of Br, Cl, and I; R¹ is independently alkyl,
 alkene, aryl, alkoxy, aryloxy, amine, amide, fluoroalkyl,
 fluoroaryl, alkyl ketone, aryl ketone, ester, formyl,
 5 cyano, fluoro, imide, sulfone, and thioether; the X
 halides are para to each other; and n = 0-4.

13. The method according to claim 1, wherein the
 phosphite ligand has the formula:



- 15 wherein R², R³, and R⁴ are independently selected from the
 group consisting of C₃ to C₂₂ alkyl, C₆ to C₂₄ aryl,
 alkaryl, and aralkyl.

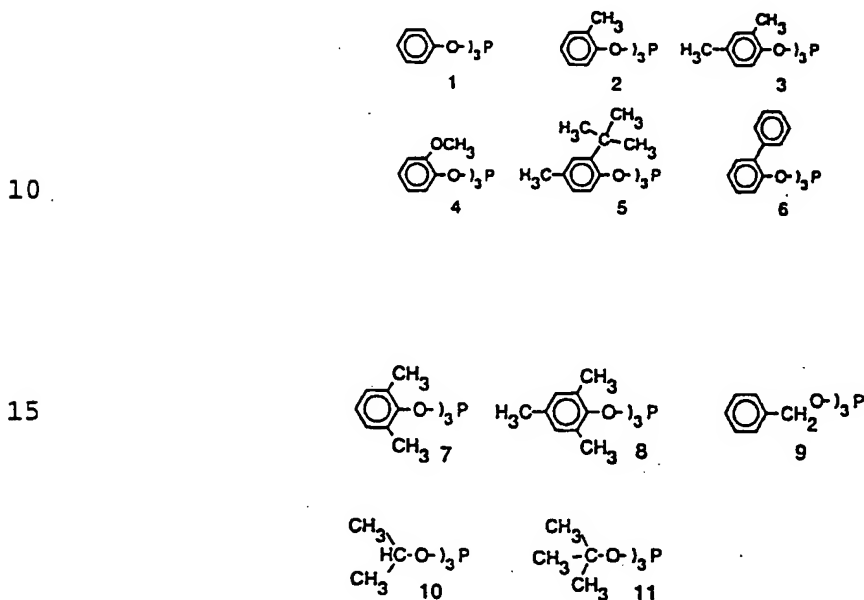
14. The method according to claim 10, wherein R²,
 20 R³, and R⁴ are independently selected from the groups
 consisting of



- 25
 30 wherein A is independently selected from the group
 consisting of C₁ - C₂₂ alkyl, C₆ - C₁₈ aryl, C₁ - C₁₂ alkoxy,
 C₆ - C₁₈ aryloxy, and F, and wherein l = 0-5, m = 0-7, n =

1 0-9, and o = 0-21; the A groups can be on any of the fused
or multiple rings; and q = 0-3.

5 15. The method according to claim 11, wherein the
phosphite ligand is selected from the group consisting of:



25 16. The method according to claim 1, wherein the
phosphite ligand is:



35 the nickel compound is nickel (II) chloride, and the
reducing metal is zinc.

1 17. The method according to claim 1, wherein the
aryl halide is 2,5 dichlorobenzophenone, the nickel
compound is nickel (II) chloride, the phosphite is tri(2-
5 methylphenyl)phosphite, the reducing metal is zinc, and
the aprotic solvent is selected from the group consisting
of N-methylpyrrolidinone (NMP), N,N-dimethylacetamide,
N-cyclohexylpyrrolidinone, dimethylformamide, and N,N,N,N-
tetramethylurea.

10 18. The method according to claim 1, wherein the
aryl halide is N-(4-chloro-2-benzoylphenyl)succinimide,
the aprotic solvent is NMP, the nickel compound is nickel
(II) chloride, the phosphite is tri(2-
15 methylphenyl)phosphite, and the reducing metal is zinc.

 19. The method according to claim 1, wherein the
aryl halide is 4-chlorotoluene, the aprotic solvent is
NMP, the nickel compound is nickel (II) chloride, the
phosphite is tri(2-methylphenyl)phosphite, and the
20 reducing metal is zinc.

 20. The method according to claim 1, wherein the
aryl halide is 2-chlorobenzophenone, the aprotic solvent
is NMP, the nickel compound is nickel (II) chloride, the
25 phosphite is tri(2-methylphenyl)phosphite, and the
reducing metal is zinc.

 21. The method according to claim 1, wherein the
aprotic solvent is an amide solvent selected from the
30 group consisting of N-methylpyrrolidinone, N,N-
dimethylacetamide, N-cyclohexyl-pyrrolidinone, and
dimethylformamide.

1 22. The method according to claim 2, wherein the
chloride, bromide, and iodide ions are introduced as salts
selected from the group consisting of alkali salts,
alkaline earth salts, alkylammonium salts, aluminum salts,
5 manganese salts, and zinc salts.

 23. The method according to claim 1, wherein the
nickel compound is selected from the group consisting of
nickel (II) chloride and nickel (II) bromide.
10

 24. The method according to claim 1, wherein the
phosphite ligand is an aryl phosphite.

 25. The method according to claim 1, wherein the
15 phosphite ligand is tri-2-tolylphosphite.

 26. The method according to claim 1, wherein the
phosphite ligand is triphenylphosphite.

20 27. The method according to claim 1, wherein the
phosphite ligand is tri-(2,4-dimethylphenyl)phosphite.

 28. The method according to claim 1, wherein the
phosphite ligand is tri-(2-methoxyphenyl)phosphite.
25

 29. The method according to claim 1, wherein the
phosphite ligand is tri-(2-tert-butyl-4-methyl-
phenyl)phosphite.

30 30. The method according to claim 1, wherein the
phosphite ligand is tri-(2-phenylphenyl)phosphite.

1 31. The method according to claim 1, wherein the
aryl halide is 6-chloro-2-(4-fluorophenyl)-4-
phenylquinoline.

5 32. The method according to claim 1, wherein the
aryl halide is a protected form of 2-amino-4-
chlorobenzophenone.

10 33. The method according to claim 1, wherein the
aryl halide is 4-chloroacetophenone.

 34. The method according to claim 1, wherein the
aryl halide is an aryl dihalide.

15 35. The method according to claim 1, wherein the
aryl halide is 2,5-dichlorobenzophenone.

20 36. The method according to claim 1, wherein the
aryl halide is 2,5-dichloro-4'-phenoxybenzophenone.

 37. The method according to claim 1, wherein the
aryl halide is 2,5-dichlorobiphenyl.

25 38. The method according to claim 1, wherein the
aryl halide is 2,4-dichlorobenzophenone.

30 39. The method according to claim 1, wherein the
aryl halide is provided as a mixture of aryl dihalides,
and the polyaryl product is a polyarene co-polymer.

- 1 40. The method according to claim 39, wherein one of
the aryl dihalides has the formula:

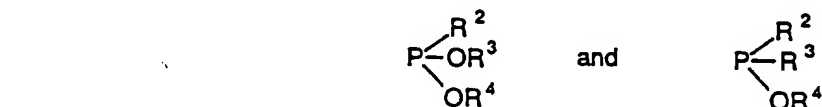


wherein X is independently selected from the group
consisting of Br, Cl, and I; R¹ is independently alkyl,
10 alkene, aryl, alkoxy, aryloxy, amine, amide, fluoroalkyl,
alkyl ketone, aryl ketone, ester, formyl, cyano, fluoro,
imide, sulfone, and thioether; the X halides are para to
each other; and n = 0-4.

- 15 41. The method according to claim 1, wherein a
mixture of two or more aryl halides is coupled.

20 42. A method of coupling aryl halides to form biaryl
or polyaryl compounds, the method comprising the steps of:
providing an aryl halide selected from the group
consisting of an aryl chloride, an aryl bromide, an aryl
iodide and mixtures thereof; and

contacting the aryl halide in an anhydrous
aprotic solvent with a catalyst mixture comprising a
25 nickel compound, a ligand selected from the group
consisting of:



1 wherein R², R³, and R⁴ are independently selected from the
group consisting of C₁ to C₂₂ alkyl, C₆ to C₂₄ aryl,
alkaryl, and aralkyl, and a reducing metal to thereby form
said biaryl or polyaryl compound.

5

43. A catalyst composition comprising a nickel
compound, a phosphite ligand, and a reducing metal
selected from the group consisting of aluminum, magnesium,
and zinc, wherein the molar ratio of ligand to nickel is
10 between 1 and 10, and the molar ratio of reducing metal to
nickel is between 1 and 10,000.

44. The composition of claim 43, wherein the
phosphite ligand is tri-2-tolylphosphite and the reducing
15 metal is zinc.

45. The composition of claim 43, wherein the molar
ratio of phosphite ligand to nickel is between 2 and 10.

20 46. The composition of claim 43, wherein said
phosphite ligand is selected from the group consisting of
triphenyl phosphite, tri-2,6-dimethylphenyl phosphite,
tri-2-phenylphenyl phosphite, tri-2-methoxyphenyl
phosphite, tri-n-butyl phosphite, tripentylphosphite,
25 tribenzylphosphite, tri-isopropylphosphite, tri-2-tert-
butylphenylphosphite, trinaphthylphosphite, tri-(2,4-
dimethylphenyl)phosphite, tri-(2,4,6-trimethyl-
phenyl)phosphite, and tri-(2-tert-butyl-4-methyl-
phenyl)phosphite.

30

47. The composition of claim 43, wherein said
phosphite is selected from the group consisting of tri C₁-
C₂₂ alkyl phosphites, tri C₆-C₂₄ aryl phosphites,

1 triaryalkyl phosphites, and mixed alkyl, aryl, and
aryalkyl phosphites.

48. A method of coupling aryl halides to form biaryl
5 or polyaryl compounds, the method comprising the steps of:

a) providing an aryl halide selected from the
group consisting of an aryl chloride, an aryl bromide, and
an aryl iodide;

b) preparing a mixture comprising the aryl
10 halide, a nickel compound or complex and a phosphite
ligand in an anhydrous aprotic solvent containing an
electrolyte;

c) placing the mixture in an electrochemical
cell comprising a cathode; and

15 d) cathodically reducing the aryl halide to
thereby form said biaryl or polyaryl compound.

49. A method of coupling aryl halides or aryl
sulfonates to form biaryl or polyaryl compounds, the
20 method comprising the steps of:

providing an aryl halide or aryl sulfonate
selected from the group consisting of an aryl chloride, an
aryl bromide, an aryl iodide, an aryl methanesulfonate, an
aryl phenylsulfonate, an aryl tolylsulfonate, an aryl
25 trifluoromethanesulfonate, an aryl fluorophenylsulfonate,
and an aryl fluorosulfonate,; and

contacting the aryl halide or aryl sulfonate in
an anhydrous aprotic solvent with a catalyst mixture
comprising a nickel compound, a phosphite ligand, and a
30 reducing metal to thereby form said biaryl or polyaryl
compound.

AMENDED CLAIMS

[received by the International Bureau on 4 October 1996 (04.10.96);
original claims 1, 2, 42, 43, 48, and 49 amended;
remaining claims unchanged (4 pages)]

1

1. A method of coupling aryl halides to form biaryl
or polyaryl compounds, the method comprising the steps of:
5 providing an aryl halide selected from the group
consisting of an aryl chloride, an aryl bromide, and an
aryl iodide; and

mixing the aryl halide in an anhydrous aprotic
solvent with a nickel compound or a nickel complex, a
10 phosphite ligand, and a reducing metal to thereby form
said biaryl or polyaryl compound.

2. The method according to claim 1, wherein the
catalyst mixture additionally comprises a promoter
15 selected from the group consisting of chloride, bromide,
and iodide salts is also mixed with the aryl halide.

3. The method according to claim 2, wherein the
promoter is sodium iodide.
20

4. The method according to claim 2, wherein the
promoter is sodium bromide.

5. The method according to claim 1, wherein the
25 phosphite ligand to nickel molar ratio is in the range of
2 to 10.

6. The method according to claim 1, wherein the
phosphite ligand to nickel molar ratio is in the range of
30 2.4 to 5.

7. The method according to claim 1, wherein the
reducing metal is selected from the group consisting of

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- 1 40. The method according to claim 39, wherein one of
the aryl dihalides has the formula:



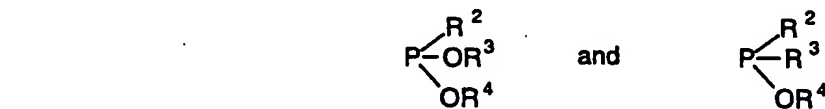
10 wherein X is independently selected from the group
consisting of Br, Cl, and I; R¹ is independently alkyl,
alkene, aryl, alkoxy, aryloxy, amine, amide, fluoroalkyl,
alkyl ketone, aryl ketone, ester, formyl, cyano, fluoro,
imide, sulfone, and thioether; the X halides are para to
each other; and n = 0-4.

15

41. The method according to claim 1, wherein a
mixture of two or more aryl halides is coupled.

20 42. A method of coupling aryl halides to form biaryl
or polyaryl compounds, the method comprising the steps of:
providing an aryl halide selected from the group
consisting of an aryl chloride, an aryl bromide, an aryl
iodide and mixtures thereof; and

25 mixing the aryl halide in an anhydrous aprotic
solvent with a nickel compound or nickel complex, a ligand
selected from the group consisting of:



30

35

1 wherein R², R³, and R⁴ are independently selected from the
group consisting of C₃ to C₂₂ alkyl, C₆ to C₂₄ aryl,
alkaryl, and aralkyl, and a reducing metal to thereby form
said biaryl or polyaryl compound.

5

43. A catalyst composition formed by mixing together
in an anhydrous aprotic solvent a nickel compound, a
phosphite ligand, and a reducing metal selected from the
group consisting of aluminum, magnesium, and zinc, wherein
10 the molar ratio of ligand to nickel is between 1 and 10,
and the molar ratio of reducing metal to nickel is between
1 and 10,000.

44. The composition of claim 43, wherein the
15 phosphite ligand is tri-2-tolylphosphite and the reducing
metal is zinc.

45. The composition of claim 43, wherein the molar
ratio of phosphite ligand to nickel is between 2 and 10.

20

46. The composition of claim 43, wherein said
phosphite ligand is selected from the group consisting of
triphenyl phosphite, tri-2,6-dimethylphenyl phosphite,
tri-2-phenylphenyl phosphite, tri-2-methoxyphenyl
25 phosphite, tri-n-butyl phosphite, tripentylphosphite,
tribenzylphosphite, tri-isopropylphosphite, tri-2-tert-
butylphenylphosphite, trinaphthylphosphite, tri-(2,4-
dimethylphenyl)phosphite, tri-(2,4,6-trimethyl-
phenyl)phosphite, and tri-(2-tert-butyl-4-methyl-
30 phenyl)phosphite.

47. The composition of claim 43, wherein said
phosphite is selected from the group consisting of tri C₃-

35

1 C₂₂ alkyl phosphites, tri C₆-C₂₄ aryl phosphites,
triaryalkyl phosphites, and mixed alkyl, aryl, and
aryalkyl phosphites.

5 48. A method of coupling aryl halides to form biaryl
or polyaryl compounds, the method comprising the steps of:
providing an aryl halide selected from the group
consisting of an aryl chloride, an aryl bromide, and an
aryl iodide;

10 mixing together the aryl halide, a nickel
compound or nickel complex and a phosphite ligand in an
anhydrous aprotic solvent containing an electrolyte;

placing the mixture in an electrochemical cell
comprising a cathode; and

15 cathodically reducing the aryl halide to thereby
form said biaryl or polyaryl compound.

49. A method of coupling aryl halides or aryl
sulfonates to form biaryl or polyaryl compounds, the
20 method comprising the steps of:

providing an aryl halide or aryl sulfonate
selected from the group consisting of an aryl chloride, an
aryl bromide, an aryl iodide, an aryl methanesulfonate, an
aryl phenylsulfonate, an aryl tolylsulfonate, an aryl
25 trifluoromethanesulfonate, an aryl fluorophenylsulfonate,
and an aryl fluorosulfonate,; and

mixing the aryl halide or aryl sulfonate in an
anhydrous aprotic solvent with a nickel compound or nickel
complex, a phosphite ligand, and a reducing metal to
30 thereby form said biaryl or polyaryl compound.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/05378

A. CLASSIFICATION OF SUBJECT MATTER IPC(6) : C08G 61/10 US CL : 528/397; 502/162; 205/67 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 528/397; 502/162; 205/67 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, A 5,102,971 (HIMMLER ET AL) 07 April 1992, see the abstract.	1-48
A	US, A, 4,326,989 (COLON ET AL) 27 April 1982, see the abstract	1-48
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* "A"	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance	"I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
* "E"	earlier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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* "O"	document referring to an oral disclosure, use, exhibition or other means	"G" document member of the same patent family
* "P"	document published prior to the international filing date but later than the priority date claimed	
Date of the actual completion of the international search 09 JULY 1996		Date of mailing of the international search report 15 AUG 1996
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